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Is Oral Finasteride Effective in Reversing Hair Loss in Men with Androgenetic Alopecia?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW in Partial Fulfillment of the

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ABSTRACT

OBJECTIVE: The objective of this selective EBM review is to determine whether or not oral finasteride is effective in reversing hair loss in men with androgenetic alopecia.

STUDY DESIGN: Review of two double blind, randomized controlled trials (RCTs), and one randomized open-label study published between 2009 and 2013, all in English language. The articles compared oral finasteride to a placebo, topical finasteride, and Serenoa repens, respectively.

DATA SOURCES: The two double-blind, randomized controlled trials (RCTs), and one randomized open-label study were found using PubMed. All articles were published in peer-reviewed journals and selected based on correlation to topic choice, date of publication, and evaluating POEMs.

OUTCOMES MEASURED: Patient reported satisfaction with therapy, change in staging from baseline as measured by the Hamilton and the Hamilton-Norwood Classification Scale for androgenetic alopecia, and change in mean size of alopecia from baseline (cm).

RESULTS: The three studies used in this review demonstrated inconsistent data on the effectiveness of oral finasteride for reversing hair loss in men with androgenetic alopecia. Rossi et al. demonstrated a statistically significant change in hair growth reversal in men taking oral finasteride when compared to Serenoa repens (P=0.013). Gubelin Harcha et al found statistically significant data that men treated with oral finasteride perceived they had increase in hair growth at the end of the trial when compared to the placebo. However, Gubelin Harcha et al found statistically insignificant data to support that men were overall satisfied with hair growth at the end of the trial (P=0.084). Hajheydari et al. demonstrated oral finasteride was statistically insignificant in reversing hair loss in men when compared to topical finasteride.

KEY WORDS: finasteride, androgenetic alopecia

INTRODUCTION

Male androgenetic alopecia, also known as male pattern balding, is the most common cause of hair loss in men.[1] Androgenetic alopecia is a condition that affects the hair follicles, resulting in a pattern of hair thinning and hair loss. It is characterized by a progressive transformation of terminal hair into villus hair. [1,2] The age of onset for androgenetic alopecia in men is generally in the late teens and early twenties but varies, and prevalence has been found to increase with age. Approximately 80% of men above the age of 60 are affected, and roughly 16% of men ages 18-29 and 53% of men ages 40-49 exhibit moderate to extensive androgenetic alopecia. [1,3,4] The disorder is around 4 times more common in Caucasian men than in African American men. When compared to Caucasian men, androgenetic alopecia affected men of Chinese origin less frequently and at a later age. In men of Japanese origin, the age of onset of androgenetic alopecia was found to be approximately 10 years after that of Caucasian men.[4]

Male pattern balding is believed to have both an endocrine and genetic component. The main hormone that is linked to androgenetic alopecia is testosterone, specifically dihydrotestosterone (DHT), and active metabolite of testosterone. [1-6] DHT is converted from testosterone by the enzyme 5-alpha-reductse.[1-6] There are two isoforms of 5-alpha-reductase that are able to convert testosterone to DHT, Type 1 and Type 2.[2,4-6] Type 1 is mostly found in the hair follicles and the sebaceous glands of the skin, whereas Type 2 is generally found in the inner root sheath of hair follicles and the male genitalia and prostate.[4,6] Higher concentrations of 5-alpha-reductase in the body are linked with androgenetic alopecia in men.[2]

Evidence suggests that androgenetic alopecia also has a familial component and polygenic inheritance.[1,2] Twin studies show an 80% predisposition to hair loss. Polygenic inheritance is also supported by evidence that there is an increased risk for androgenetic alopecia

in families with increased number of affected individuals[2]. This is thought to be due to an abnormality of the androgen-receptor gene on the X-chromosome, which would lead to maternal inheritance of androgenetic alopecia, as well as a mutated locus on chromosome 3.[2]

Current FDA approved medications for hair restoration due to androgenetic alopecia include topical minoxidil (Rogaine) and oral finasteride.[1,2,6] Other off-label medications used to help reverse hair loss are dutasteride, latanoprast, and topical finasteride.[2,5] Hair transplant surgery is also an effective therapeutic option for long-term treatment of androgenetic alopecia.[1,2,4] It is estimated that millions of dollars are spent annually on products to help reverse hair loss.[4]

Objective

The objective of this selective EBM review is to determine whether or not oral finasteride is effective in reversing hair loss in men with androgenetic alopecia (male pattern baldness).

Method

Two randomized control studies and one randomized open label study were used in this review. These studies consisted of men ages 18 and older diagnosed with androgenetic alopecia. Gubelin Harcha et al. compared the effectiveness of 4 control groups receiving either 0.02mg, 0.1 or 0.5mg/day of dutasteride or a placebo, and an experimental group receiving 1mg/day of finasteride. Each of the 5 groups received their randomly assigned medication daily for a total of 24 weeks. At the 12th and 24th week of the experiment, a 3-question Hair Growth Index (HGI) questionnaire was given to each participant to assess their subjective perception of their amount of hair. The HGI included a 7-point scale that ranged from "much less hair" to "much more

hair". Each participant was also given a 5-question Hair Growth Satisfaction Scale (HGSS) which was administered at 12 and 24 weeks to assess the participants' satisfaction. The HGSS also had a 7-point scale that ranged from "very dissatisfied" to "very satisfied". Gubelin Harcha et al. also used the Hamilton-Norwood Classification Scale to assess each participant's change in stage of androgenetic alopecia at the end of the 24-week trial. The change in each participant's staging was used to assess their therapeutic response. The secondary outcomes measured in this study were hair growth, change in terminal hair count, and an investigator photographic assessment questionnaire; however, these outcomes are not addressed in this paper.[6]

Hajheydari et al. conducted a double-blind randomized clinical trial to compare the effectiveness of a control group of topical finasteride gel with an experimental group receiving 1 mg of finasteride per day by mouth. Effectiveness of treatment was evaluated by comparing change in the size of alopecia in centimeters for both groups at the end of the 6-month trial and the overall effectiveness of each therapy measured after each month. Secondary outcomes measured in this study were hair count and change in number of terminal hairs at the end of the study; however; these secondary outcomes are not considered POEMS and will not be addressed in this paper.[5]

Rossi et al. conducted a randomized open label study comparing a control group of *Serenoa repens*, a plant also known as saw palmetto, with the experimental group of oral finasteride for the treatment of male androgenetic alopecia. This experiment measured the outcomes of each therapy for 24 months. Outcomes were measured by comparing the Hamilton Classification scores of each participant at the beginning of the trial to their score at the end of the 24 months. The subjective therapeutic effectiveness for both therapies was also evaluated by three dermatologists, however these outcomes are not reviewed in this paper.[3]

The studies above were found using PubMed. The keywords used for PubMed were finasteride and alopecia. Articles that evaluated outcomes that measured patient oriented evidence that matters (POEM's) from 2007-2017 were selected. The population studied was men ages 18 and older that have androgenetic alopecia. Populations excluded were women, children under the age of 18, and those with hair loss due to etiologies other than androgenetic alopecia. The statistics reported in these articles were p-values ($p<0.05$ were considered clinically significant), number needed to treat, and mean change from baseline. Table 1 shows the demographics and characteristics of the included studies.

Outcomes Measured

The patient oriented outcomes measured in these trials were patient satisfaction with the therapy at the end of the trial, mean change in size of alopecia, subjective overall effectiveness of therapy at the end of the trial, and overall change in rating of alopecia based on the Hamilton Classification Scale for androgenetic alopecia. Gubelin Harcha et al. used the Hamilton-Norwood Classification Scale to evaluate change in the participants' baseline androgenetic alopecia to assess their response to therapy at the end of 24 weeks. They also used a 3-qusetion survey and a 5-question survey at the 12^{th} and 24^{th} week to assess to the participants' perception of the therapeutic effectiveness of the randomly assigned medication they received. Hajheydari et al. compared the size of the area of alopecia (cm) before and after the trial was conducted. Rossi et al. used the Hamilton Classification Scale to compare each participants' stage of androgenetic alopecia from before the trial to their staging at the end of the trial. The change in staging was used to assess the participant's response to therapy.

Table 1: Demographics and Characteristics of included studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Gubelin[1]	Double Blind RCT	917	Men 20-50	-Alopecia type III vertex, IV, V (based off Hamilton-Norwood scale) -Maintain same hair color & style	-serum testosterone less than 250 ng/dL -unstable liver disease -h/o malignancy within prior 5 yrs -prostate CA in 1st degree -PSA > 2.0 ng/ML -hair loss not caused by androgenetic alopecia -any condition/disease of scalp/hair	156	PO finasteride 1.0 mg/d x 6 months
Hajheydari[2]	Double Blind RCT	45	Men Under 30	-Males < 30 with androgenetic alopecia Hair loss less than 5 yrs -max diameter of hair loss less than 10cm	-Males with androgenetic alopecia who are under treated -males with baseline disease that causes hair loss	7	PO finasteride 1.0mg/d x 6 months
Rossi [3]	Randomized open label study	100	Men 20-40	Mild to moderate androgenetic alopecia based on Hamilton classification	-Surgical alteration of scalp -topical minoxidil use in previous year -Men with alopecia as result of other causes	0	PO finasteride 1.0mg/d x 24 months

Results

The double-blind randomized clinical trial conducted by Gubelin Harcha et al. included 917 men between the ages 20-50 years old. Of the 917 men participating, 761 completed the trial. Twenty-one withdrew from the trial due to adverse events, 9 due to protocol deviation, 48 participants were lost to follow up, 20 were released at investigator discretion, and 58 withdrew consent. All of the participants were diagnosed with androgenetic alopecia and were classified as either type III vertex, IV, or V based of the Hamilton-Norwood Classification Scale. Participants were randomly assigned to either one of the four control groups (Placebo, dutasteride 0.02mg/day PO, dutasteride 0.1mg/day PO, dutasteride 0.5mg/day PO) or the experimental group (finasteride 1mg/day PO). 181 participants were randomly assigned to the placebo group, 185 participants were assigned to dutasteride 0.02mg/day PO, 188 were assigned Dutasteride 0.1mg/day PO, 184 were assigned dutasteride 0.5mg/day PO, and 179 were assigned finasteride 1mg/day PO. This review focused on using the placebo as the control group with 1mg oral finasteride as the experimental group.[6]

Using the Hamilton-Norwood Classification scale for androgenetic alopecia, participants were classified at the end of 24 weeks as either worsening in stage, unchanged stage, or improvement in stage. To dichotomize the data found in Table IV of Gubelin Harcha et al., this review classified participants as either improved from baseline or unimproved from baseline at the end of 24 weeks. This data is found in Table IV of Gubelin Harcha et. al. Table 2 shows the control event rate (CER), experimental event rate (EER), relative benefit increase (RBI), absolute benefit increase (ABI), and the calculated numbers needed to treat (NNT).[6]

Gubelin Harcha et al. also used a 3 question HGI and a 5 question HGSS to assess participants satisfaction with the therapy they received. At week 24, participants receiving 1mg

tablet of finasteride had a mean increase of 2.5 and participants receiving the placebo had a mean increase of 1.1 on the HGI score (P< .001), a finding that is statistically significant. Participants receiving finasteride had a mean increase of 10.1 on the HGSS, while participants receiving the placebo had a mean increase in 9.1 on the HGSS (P = 0.084), which is statistically insignificant.[6]

Table 2. Baseline Change in Hamilton-Norwood Classification in Gubelin Harcha et. al.

CER	EER	RBI	ABI	NNT
0.185	0.267	0.443	.082	13

The double-blind randomized control study conducted by Hajheydari et al. included 45 men between the ages of 18 and 35 years old clinically diagnosed with androgenetic alopecia. Of the 45 men, 7 participants were excluded from the trial. Participants were randomly divided into two groups. Group A received topical finasteride gel and a placebo tablet. Group B received a placebo gel and an oral tablet of finasteride 1mg. Participants were instructed to take their assigned tablet once daily and apply their assigned topical gel twice daily.

Hajheydari et al. measured the size of alopecia (cm^2) of participants before and after the 6-month trial. Before the trial, the average size of alopecia in participants taking oral finasteride 1mg daily was 7.55 cm with a standard deviation of 2.28cm. At the end of the 6-month trial, the average size of alopecia was recorded as 7.18cm with a standard deviation of 2.17cm. The p-value was found to be 0.07, which is statistically insignificant. Table 3 shows the mean change from baseline in participants using oral finasteride and topical finasteride.[5]

Table 3: Average Change in Size of Alopecia in Hajheydari et al.

	Finasteride Tablet Baseline	Finasteride gel baseline	Finasteride tablet at 24 months	Finasteride gel at 24 months
Size of alopecia (cm)	7.55	7.21	7.18	6.72
Standard Deviation	2.28	2.08	2.17	2.41
p-value	0.07		0.08	

Rossi et al. conducted a randomized open label study with 100 men diagnosed with androgenetic alopecia, all completing the trial. The participants were equally separated into two groups and treated with oral finasteride 1mg/day or *Serenoa repens* 320 mg/day. In Table IIIa of Ross et al. the results of the Hamilton Classification score to assess the hair growth of participants treated with oral finasteride at the end of 24 months. Rossi et al. classified participants as worsened, stable, or improved based of their Hamilton Classification at the end of the 24-month trial is shown.* This review dichotomized the data by classifying the participants as either improved or unimproved. The unimproved category includes both the worsened and stable classifications by Rossi et. al. Of the 50 participants treated with finasteride, 34 were categorized as improved, and 16 were categorized as worsened or stable. A chi-square of 6.09 and a p-value of 0.013 were reported for this data and show that the data is significantly significant. Table 4 of this review shows the CER, EER, RBI, ABI, and NNT of the trial conducted by Rossi et al.[3]

Table 4. Therapeutic response of oral finasteride compared to Serenoa repens by Rossi et al.

CER	EER	RBI	ABI	NNT
0.38	0.68	0.79	.30	4

Discussion

Finasteride is a 5-alpha reductase inhibitor that was approved in 1997 by the FDA to treat androgenetic alopecia[4]. The two randomized control trials and the one randomized open label study discussed in this paper examined the therapeutic advantage of oral finasteride in reversing hair loss in adult men diagnosed with androgenetic alopecia.

When compared to a placebo in Gubelin Harcha et al., oral finasteride was found to have a NNT of 13, which represents a large treatment effect. A NNT of 13 means that for every 13 patients treated with 1 mg/day of PO finasteride, one patient with androgenetic alopecia will experience an improvement of hair growth. Participants treated with finasteride showed a statistically significant subjective improvement in their amount of hair at the end of the 24-week trial. The p-value for the HGSS was greater than 0.05, indicating that participants treated with oral finasteride did not have significant improvement in satisfaction of therapy when compared to the placebo. One limitation of this study is the use of subjective questionnaires to assess therapeutic effectiveness of interventions, as participants may have different expectations of outcomes of therapy. Other limitations of this study are only including men between the ages of 20 to 50 years old, and the short duration of the trial.

The study conducted by Hajheydari et al. showed finasteride did not have significant improvement in hair growth when compared to topical finasteride gel. Limitations of this study include the number participants, only including men under the age of 30, and excluding male with androgenetic alopecia for over 5 years.

Rossi et al. found a significant improvement in hair growth for participants taking oral finasteride when compared to Serenoa repens. This study found a NNT of 4, meaning that for every 4 patients treated with finasteride, 1 will show improvement in hair growth in men with androgenetic alopecia. Limitations of this study include using only men between the ages of 20 and 40, using an open-label study, and comparing finasteride with a plant extract that is not FDA approved for the treatment of androgenetic alopecia in men.

Conclusion

The two randomized control trials and one randomized open label study examined in this review showed inconsistent data on whether or not 1mg of oral finasteride was effective in reversing hair loss in men with androgenetic alopecia. Future studies should consider investigating the effect finasteride has on hair loss for a longer duration, on populations younger than 18 who have been diagnosed with androgenetic alopecia, effectiveness of different doses of PO finasteride, and the effect PO finasteride has on women suffering from androgenetic alopecia. This review studied the effectiveness of oral finasteride in reversing hair loss in men with androgenetic alopecia.

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